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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/554,424	11/06/95	VAN DER PLOEG	19330DA

MERCK AND COMPANY INC
PATENT DEPARTMENT
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EXAMINER
LUBET, M

ART UNIT	PAPER NUMBER
1016	

10/28/97
DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/554,424	Applicant(s) VAN DER PLOEG
	Examiner Lubet	Group Art Unit 1816

Responsive to communication(s) filed on Jul 21, 1997

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 20-26 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 20-26 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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1. This office action is in response to paper 9 filed July 21, 1997.
2. Examiner acknowledges the cancellation of claims 1-16 in the above mentioned paper 9. Newly added claims 20-26 are under examination.
3. The text of those section of Title 35, U.S.C. not included in this action can be found in a prior office action.
4. The rejection of claims 3-6 under 35 U.S.C. § 112, second paragraph set forth in Section 7 of Paper 7 mailed January 23, 1997 is withdrawn because claims 3-6 are canceled.
5. The rejection of claims 3-6 under 35 U.S.C. § 112, first paragraph set forth in Section 8 of Paper 7 mailed January 23, 1997 is withdrawn because these claims are canceled.
6. The rejection of claims 3-6 under 35 U.S.C. 103(a) set forth in Section 9 of Paper 7 mailed January 23, 1997 is withdrawn because claims 3-6 are canceled.
7. New rejections under 35 U.S.C. 112, second paragraph necessitated by amendment.

Claims 20-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 20, it is unclear if the cell in which para and tipE are expressed lacks a voltage-activated sodium channel prior to the induction of expression of para and tipE gene products. If so, what cells lack a voltage-activated sodium channel?

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B. In claims 20-26, it is unclear what the term "para" means. The claims would read more clearly if the claim identified "para" as a temperature sensitive mutant paralytic mutation of sodium channel in Drosophila.

C. In claims 20-26, it is unclear what the term "tipE" means. The claims would read more clearly if the claim identified "tipE" as a temperature sensitive mutant paralytic mutation of sodium channel in Drosophila.

D. In claim 22, it is unclear what the term "are introduced into the host cell" means. Does this term encompass injection of isolated DNA molecules encoding para and tipE genes into the cells and transfection of vectors which comprise para and tipE genes? If the claim language encompasses transfection of vectors which comprise para and tipE genes, must the para and tipE genes be in the same vector or does the claim language encompass co-transfection with two vectors, one comprising para gene and the other the tipE gene?

8. New rejections of claims 20-26 under U.S.C. §103(a) necessitated by amendment.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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10. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jackson et al (D) (J. of Neurogenetics 3: 1, 1986) in view of O'Dowd et al (J) (J. Of Neuroscience 8:3633, 1988).

A. Jackson et al. teach double Drosophila mutants expressing para^{ts-1} and tipE (see pages 10-11, in particular). Thus cells isolated from these double mutants express para and tipE and are from a multicellular organism. Jackson et al. does not disclose a method of identifying ligands that modulate Drosophila membrane sodium channels. However, O'Dowd et al. teach a method of identifying ligands that modulate sodium channel in Drosophila neurons of tipE mutant Drosophila *in vitro* by measuring the ability of ligands such as tetrotoxin to modulate the voltage-activated current (see Figure 6 and pages 3637, in particular). Therefore it would have been *prima facie* obvious to one with skill at the time of the invention to substitute cells from the para/tipE double mutant taught by Jackson et al. for the tipE mutant cells used in the assay taught by O'Dowd et al. with the expectation that the assay would identify ligands that modulate the Drosophila membrane sodium channel.

11. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacKinnon et al. (UU) (Neuron 5, 767, 1990) in view of Jackson et al. (D) and further in view of Loughney et al. (M) (Cell 58: 1143, 1989) and Hall et al. (H) (in Drosophila, 35th Annual Drosophila Res. Conference vol. 77, April, 1994).

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A. MacKinnon et al. teach a method of identifying ligands that modulate a Drosophila membrane sodium channel which comprises expressing RNA or cDNA of wild-type or Shaker mutants by injecting the RNA or DNA into Xenopus oocytes and measuring the ability of ligands such as charbodotoxin to modulate voltage-activated current (see Figure 2 and Table 1 and pages 767 and pages 770-771, in particular) in the cells injected with RNA or cDNA encoding wild type or mutant sodium channel proteins.

B. MacKinnon et al. do not teach the injection of RNA or cDNA that encodes the para and tipE mutants into Xenopus oocytes, however, as discussed supra, Jackson et al. teach the use of para/tipE double mutant Drosophila to study the physiology of interaction of para/tipE mutants. Jackson et al. do not teach the isolated RNA or DNA encoding para locus protein or tipE protein. However, Loughney et al. teach the genomic and cDNA of para locus of Drosophila (see Figures 2-5 and pages 1148-152, in particular). Hall et al. teach an isolated cDNA that encodes for the tipE mutation (see entire abstract).

Therefore one with skill in the art at the time of the invention would be motivated to substitute the isolated RNA or DNA encoding the para and tipE mutant proteins taught by Loughney et al. and Hall et al. for the RNA or DNA encoding sodium channel proteins used in the method of MacKinnon et al. to identify ligands that modulate Drosophila membrane sodium channels since Jackson et al. teaches that the interaction of para and tipE mutation can be studied when para and tipE mutants are expressed as double mutants.

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12. A prior art search of the embl-new3, EST-STS and geneseq27 data bases does not reveal a DNA with the exact sequence as SEQ ID. NO. 7. However, SEQ ID NO. 7 differs from the para sequence taught by Loughney et al. only in residues 3613-3815 which correspond to residues 3367-3612 of SEQ ID. No. 7. Therefore claims 24-26 are free of the prior art.

13. Examiner believes that all pertinent arguments have been addressed.

15. No claim is allowed. THIS ACTION IS MADE FINAL since the new grounds of rejection are necessitated by amendment. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Martha Lubet in Art Unit 1816 whose telephone number is (703) 305-7148.

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The examiner can normally be reached on Monday through Friday from 8:15 AM to 4:45 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-3014. The FAX number for this group is (703) 305-3014 or 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Martha T. Lubet

October 20, 1997

TC

THOMAS M. CUNNINGHAM
PRIMARY EXAMINER
GROUP 1800